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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/109,082	07/02/98	MELKI J	2121-140P

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EXAMINER	
HAYES, R	
ART UNIT	**PAPER NUMBER**
1647	20

DATE MAILED: 09/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/109,082	Melki et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 27, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *21, 23, 30-34, 36, and 40-65* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *21, 23, 30-34, 36, and 40-65* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Response to Amendment

1. The amendment filed 6/27/01 has been entered.

2. The objection of claim 33 under 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification **and claims** is withdrawn due to the amendment of the claim.

3. The rejection of claims 36 & 40-52 under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling, as it relates to information critical or essential to the practice of the invention, but not included in the claim(s), is withdrawn due to the amendment of the claims.

4. The rejection of claims 21-23 & 30-32 under 35 U.S.C. 112, second paragraph, as being indefinite for being dependent on non-elected base claims is withdrawn due to the amendment of the claims.

5. The rejection of claims 23, 30-32, 36, 40, 48 & 50 under 35 U.S.C. 112, second paragraph, as being indefinite for what the recitations "SCCP", or "SMA" entail is withdrawn due to the amendment of the claims.

6. Applicant's arguments filed 6/27/01 have been fully considered but they are not deemed to be persuasive.

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. The oath or declaration remains defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. In contrast to Applicants' assertions, the citizenship of not a single inventor is identified.

9. Claims 23, 30-32, 53 & 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No proper antecedent basis nor conception in context with that described within the specification at the time of filing the instant application is apparent for the recitation, "a Survival Motor Neuron disorder"(i.e., as it relates to claims 30-32 & 65); thereby, constituting new matter.

No proper antecedent basis nor conception in context with that described within the specification at the time of filing the instant application is apparent for the recitation, "comprises

at least 9 nucleotides within... SEQ ID NO:21", versus SEQ ID NOs: 12 or 13 of Figure 3 (i.e., as it relates to claims 23 & 53); thereby, constituting new matter. Moreover, the hybridization products of claim 53 (i.e., original claim 22) are not contemplated for SEQ ID NO:21; thereby, further constituting new matter.

10. Claims 21, 23, 30-34, 36, 40-52 & new claims 53-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting specific motor disease states related to specific mutations of specific nucleotide sequences (i.e., by SEQ ID NO) using structurally definable probes or pairs of probes (i.e., by SEQ ID NO) and known restriction enzymes to generate detectable and definable polymorphisms, does not reasonably provide enablement for any generic method that does not identify the specific disease state being detected, especially when using structurally uncharacterized probes that may or may not identify specific portions of undefined or unknown genes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons made of record in Paper No. 18, and as follows.

Applicants argue on pages 9-10 of the response that "the term 'defect' is defined on page 6", and that "the specification does enable a person skilled in the art to make and/or use the invention commensurate in scope with these kit claims as amended". In contrast to Applicants' assertions, an "example" of "defects" is not equivalent to a definition, and more importantly,

without using structurally definable probes that specifically distinguish the wildtype SMN gene from mutated forms/polymorphisms that define a "defect in the survival motor neuron gene", the skilled artisan would not know how to make and use the invention as claimed without requiring undue experimentation to discover such (i.e., as it especially related to unknown hybridization products). In other words, an invitation for others to discover how to determine what constitutes a "defect" in a putative gene/DNA fragment that is otherwise not structurally definable, or using undefinable or random probes not in pairs, etc. in order to try to make the instant invention work, is not enabled. For example, as it relates to the components required in the currently claimed 'kit", and consistent with the teachings of Rudinger previously made of record, it was held in *Ex parte Maizel* (27 USPQ2d 1662 at 1665) that:

> Appellants have not chosen to claim the DNA [product] by what it is but, rather, by what it does, i.e., encoding either a protein exhibiting certain characteristics, *or* a biologically functional equivalent thereof. Appellants' claims might be analogized to a single means claim of the type disparaged by the Court of Customs and Patent Appeals in *In re Hyatt,* 708F.2d 712, 218 USPQ 195 (Fed. Cir. 1983). The problem with the phrase "biologically functional equivalent thereof" is that it covers any conceivable means, i.e., cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA [product] segment known to the inventor. Clearly the disclosure is not commensurate in scope with the claims."

Therefore, Applicants' arguments are not persuasive for the reasons made of record.

Note, the recitation of "at least one of said primers is contained within the sequence..." does not identify what constitutes the other required primer, in order to successfully practice the claimed invention (e.g., as it relates to claims 21 & 30). Additionally, amplification reactions

require specific pairs of primers from the sense and antisense strands within sufficient proximity to generate unique and identifiable restriction fragments (i.e., as it also relates to claims 36, 57 & 64-65). Finally, claims 40 and 50 also do not appear to be workable because SEQ ID NO:21 is the amino acid sequence of mouse SMN (see page 20, Figure 13), versus a human nucleic acid sequence, in which a human disease state is not reasonably detectable through comparison of a murine amino acid sequence with a human nucleotide sequence of SEQ ID NO:13.

11. Claims 40-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, SEQ ID NO:13 defines intron 6 to exon 8, versus exons 7 and 8; thereby, being ambiguous. Identification of the appropriate nucleotide positions within SEQ ID NO:13 may obviate this rejection.

12. Claims 30-32, 36, 48 & 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record in Paper No. 18. It remains unknown what metes and bounds define SSCP, since no such SSCP conditions are recited; thereby, being incomplete. Further, it is unclear what claim 32 now entails in that base claim 30 changed/cancelled original step (d).

In contrast to Applicants' assertions on page 13 of the response, Example 10 is but an "example" of SSCP using different primers and DNA, etc., which therefore, does not define what constitutes SSCP, as claimed.

13. Claims 30-33, 36 & 65 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps, for the reasons made of record in Paper No. 18. See MPEP § 2172.01. The omitted steps are: when "detecting the presence or absence of the motor neuron disorder/AMC" (i.e., as it relates to claim 21 & 36, respectively), or when "detecting spinal muscular atrophy" (i.e, as it relates to the preamble of claim 33), is completed. In other words, what metes and bounds constitute a "defect", or "the presence or absence of AMC/SMA"? Additionally, what is the relationship between "detecting the hybrids formed" and detecting the presence of SMA in claim 33, or what definable relationship does a SSCP possess in detecting "the presence or absence of AMC" in claim 36, etc.?

14. Claims 23, 33-34 & 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record in Paper No. 18. It remains unknown what metes and bounds "stringent hybridization conditions" entail, in that it is

unknown whether low, moderate or high stringent conditions are envisioned; nor what exactly defines these conditions.

In contrast to Applicants' assertions, conditions cited in Sambrook are but examples of putative hybridization conditions, which are further not defined as low, moderate or high, and further constitute merely relative terms. Nevertheless, such a reference would constitute an inappropriate incorporation by reference, even if so stated *in arguendo*, because Sambrook is not a U.S. patent. Thus, Applicants' arguments are moot.

15. Claims 21, 43, 47-48 & 64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record in Paper No. 18. It remains unknown what metes and bounds "an amplification reaction" (e.g., as it relates to claim 21) entail, since no such conditions are recited; thereby, being incomplete.

Applicants argue on page 14 of the response that "the phrase 'amplification reaction' is perfectly clear to a skilled artisan", that "the skilled artisan will also perfectly understand the meaning of the term 'analyzing', having regard to the specification", and that "[a]lternatively, the analysis of exon 7 can be limited to the determination of whether this exon is present or not". In contrast to Applicants' assertions, the claims do not recite use of PCR or LCR, nor do they state whether exon 7 is present or not, nor do these claims "limit the determination" to such, nor do these claims state specifically how the analysis is to be preformed, including use of any specific

"enzymatic restriction or sequencing"; thereby, preventing the skilled artisan from knowing what metes and bounds such analysis entails. Thus, Applicants' arguments are not persuasive, except as it relates to claims 40, 46 & 49-50.

16. Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and lacking proper antecedent basis for the recitation of "said motor neuron disorder", since base claim 30 was amended to eliminate such proper basis.

17. Claims 23 & 40-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, SEQ ID NO:21 is an amino acid sequence versus a T-BCD541 gene.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
September 5, 2001